

Remarks

Prior to this amendment, claims 2-31, 33-41, 43-46, 49-59, and 61-64 were pending (of which claims 2-4, 7, 14, 22-24, 28-31, 33-41, 43-46, 49-59, and 61-64 are withdrawn). Claims 2-4 and 22-24 are canceled and new claims 65-73 are added. Claims 2, 12, 13, 15, 20-21 and 25 are amended herein. Claims 2 and 25 are amended to be in independent form.

Support for the amendment of claims 12, 13, 20, and 21 can be found in the specification at least at page 22, lines 3-5. Support for the amendment of claim 15 can be found in the specification at least at page 2, lines 37-39. Support for the amendment of claim 25 can be found in the specification at least at page 39, lines 12-16. Support for new claims 65-67 can be found in the specification at least at page 2, lines 1-3. Support for new claims 68-69 can be found in the specification at least at page 11, lines 5-7 and original claims 22-23. Support for new claim 70 can be found in the specification at least at page 9, lines 31-33 and support for new claim 71 can be found in the specification at least at page 2, lines 10-13. Support for new claims 72 and 73 can be found in the specification at least at page 14, line 25 through page 15, line 29; page 19, lines 1-2; page 42, lines 21-39. Of the withdrawn claims, claims 28, 31, and 33 are amended to parallel the scope of the pending claims.

No new matter is introduced by the foregoing amendments. After entry of this amendment, **claims 5-21, 25-31, 33-41, 43-46, 49-59, and 61-73 are pending (of which claims 7, 14, 28-31, 33-41, 43-46, 49-59, and 61-64 continue to be withdrawn)**. Consideration and allowance of the pending claims are requested.

Applicants thank Examiner Nguyen for acknowledging that the Information Disclosure Statements filed on October 15, 2004, February 11, 2005, and January 4, 2006 have been considered.

Election/Restrictions

Applicants acknowledge that the election of Group II (claims 5-13, 15-21, and 25-27) is made final and that claims 2-4, 7, 14, 22-24, 28-31, 33-41, 43-46, 49-59, and 61-64 are withdrawn from consideration. In addition, Applicants acknowledge that the further species

elections of SEQ ID NO: 8 (and corresponding SEQ ID NO: 37) and SEQ ID NO: 11 are made final.

Objection to the Claims

Claims 5 and 25 are objected to because they depend from a non-elected claim 2. Solely to advance prosecution in this case, claims 5 and 25 are amended to be in independent form. Applicants respectfully request that the objection to claims 5 and 25 be withdrawn in light of this amendment.

Claim Rejections Under 35 U.S.C. §101

Claims 12-13 and 20-21 are rejected under 35 U.S.C. §101 because allegedly the claimed invention is directed to non-statutory subject matter. Applicants traverse this rejection. However, solely to advance prosecution in this case, claims 12, 13, 20, and 21 are amended to be directed to an “*in vitro* host cell.” Applicants respectfully request that the rejections of claims 12, 13, 20, and 21 be withdrawn in light of this amendment.

Claim Rejections Under 35 U.S.C. §112, first paragraph (written description)

Claims 5-6 and 8-13 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection.

MPEP §2163 states the following:

The written description requirement for a claimed genus may be satisfied through *sufficient description of a representative number of species* by actual reduction to practice . . . , reduction to drawings . . . , or by *disclosure of relevant, identifying characteristics, i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics . . . Description of a representative number of species *does not require the description to be of such specificity that it would provide the individual support for each species that the genus embraces*” (emphasis added).

i) A sufficient description of a representative number of species

Applicants submit that, contrary to the assertion of the Office (Office action at page 7), the specification provides *a sufficient description of a representative number of species* in the genus of nucleic acid sequences encoding RFX4_v3 polypeptides having RFX4_v3 activity. For example, nucleic acid sequences encoding human, murine, and zebrafish RFX4_v3 polypeptides are clearly described (see, for example, the specification at page 8, line 34 through page 9, line 40; page 26, line 6 through page 31, line 36; and the sequence listing). In addition, the specification clearly describes nucleic acid sequences encoding RFX4_v3 polypeptide variants having, for example, 70%, 80%, 90%, and 95% sequence identity with SEQ ID NO: 8 (see page 29, lines 3-13; page 30, lines 24 -33) and conservative variants of SEQ ID NO: 8 (see, for example, page 31, lines 3-23). Furthermore, the specification (see, for example, page 30, line 34 through page 31, line 23) clearly describes that the variant will “function in a fashion similar to the wild-type protein” (page 31, line 22). Thus, the specification clearly includes “a sufficient description of a representative number of species” for the genus of nucleic acid sequences encoding RFX4_v3 polypeptides (including variants) having RFX4_v3 activity.

ii) Disclosure of relevant, identifying characteristics

Applicants further submit that the specification discloses a number of *relevant, identifying characteristics* of the RFX4_v3 polypeptides encoded by the claimed nucleic acid sequences that would enable one of skill in the art to readily identify members of this genus, even if they were not specifically described in the specification. For example, the specification discloses that the RFX4_v3 polypeptides encoded by the claimed nucleic acid sequences “belong to the winged-helix subfamily of helix-turn-helix transcription factors, and are so named because they bind to ‘X-boxes’.” The specification also describes that RFX members are evolutionarily conserved transcription factors that share a highly conserved winged helix DNA-binding domain, as well as a dimerization domain, and B and C boxes (specification at page 1, lines 29-31; page 32, lines 6-9; and Figure 6). These RFX conserved regions were known to those of skill in the art at the time the application was filed. Furthermore, the RFX4_v3 polypeptides are defined by a unique set of amino terminal 14 amino acids (specification at page 25, lines 29-31). Based on the conserved functional domains and the unique amino terminal sequence, one of skill in the art

would readily identify the RFX4_v3 polypeptides encoded by the claimed nucleic acid sequences. Thus, contrary to the allegations by the Office, the specification clearly describes “sufficient relevant identifying characteristics such that one of skill in the art would recognize that the inventor had possession of the claimed invention” (Office action at page 8).

iii) Does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces

MPEP §2163 states that it is not required to “*provide individual support for each species that the genus embraces*” in order to sufficiently describe the genus. Thus, Applicants submit that there is *no requirement* that all encompassed species be specifically identified in the specification. As discussed above, the specification provides *a sufficient description of representative number of species* and a number of *relevant, identifying characteristics* that sufficiently describe the genus of nucleic acid sequences encoding RFX4_v3 polypeptides. Any sequences not specifically described in the specification that fall within the claimed genus also display the identifying characteristics used to describe the existing members of the genus. Accordingly, although the specification may not disclose every member of the claimed genus, if the undisclosed possess the characteristics that define the members of the genus, then the undisclosed species are sufficiently described.

As stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960):

[I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, it may not be necessary to enumerate a plurality of species *if a genus is sufficiently identified in an application by “other appropriate language”* (emphasis added).

As discussed above, the specification discloses multiple members of the genus of nucleic acid sequences encoding RFX4_v3 polypeptides known at the time the application was filed. Although additional members of the genus are not specifically identified by name, the specification clearly uses “other appropriate language,” such as disclosing that the claimed molecules have domains found in other evolutionarily conserved RFX transcription factors, such as (i) a winged helix DNA-binding domain; (ii) a dimerization domain; and (iii) B and C boxes (specification at page 1, lines 29-31; page 32, lines 6-9; and Figure 6). The specification also

discloses that the RFX4_v3 polypeptides are further defined by a unique set of amino terminal 14 amino acids (specification at page 25, lines 29-31). Thus, based on the specification, one of skill in the art would clearly be able to identify which other proteins should be included in the genus of nucleic acid sequences encoding RFX4_v3 polypeptides.

The Office also alleges that the effects of a single nucleotide or amino acid mutation “are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations” (Office action at page 7). However, based on the known conserved domains of the claimed sequences, it was well known to those of skill in the art at the time the application was filed which residues cannot be substituted. Thus, Applicants submit that one of skill in the art could easily envision nucleic acid sequences encoding RFX4_v3 polypeptides based on the teaching of the specification, what was known in the art at the time the application was filed, and the provision of the sequences themselves.

Claim Rejections Under 35 U.S.C. §112, second paragraph

Claim 25 is rejected under 35 U.S.C. §112, second paragraph, because allegedly claim 25 is incomplete for omitting essential steps. Applicants respectfully traverse this rejection. However, solely to advance prosecution in this case, claim 25 is amended to include an expression step. Applicants respectfully request that the rejection of claim 25 be withdrawn in light of this amendment.

Claim Rejections Under 35 U.S.C. §102

Venter et al.

Claims 15-17, 19-21, and 26-27 are rejected under 35 U.S.C. §102(c) as allegedly anticipated by Venter et al. (U.S. Patent No. 6,812,339) because Venter et al. discloses a nucleotide sequence (SEQ ID NO: 416) that is 72.3% identical to the nucleotide sequence set forth as SEQ ID NO: 37. Applicants respectfully traverse this rejection. However, solely to advance prosecution in this case, claim 15 is amended to recite that the isolated nucleic acid molecule “hybridizes under conditions of low stringency to a polynucleotide consisting of nucleotides 1-42 of a nucleic acid sequence selected from the group consisting of SEQ ID NO:

37, SEQ ID NO: 38, and SEQ ID NO: 39.” As the Venter *et al.* sequence (SEQ ID NO: 416) aligns with SEQ ID NO: 37 beginning at residue 36 of SEQ ID NO: 37, the Venter *et al.* sequence does not hybridize to a polynucleotide consisting of residues 1-42 of SEQ ID NO: 37 (see sequence alignment presented with Office action), as required by amended claim 15. Thus, Venter *et al.* does not anticipate claim 15, as amended. Claims 16-17, 19-21, and 26-27 depend, directly or indirectly, from claim 15 and incorporate all of the limitations thereof. Applicants respectfully request that the rejection of claims 15-17, 19-21, and 26-27 be withdrawn in light of the current arguments and amendments.

Nakayama *et al.*

Claims 15-17, 19-21, and 26-27 are rejected under 35 U.S.C. §102(c) as allegedly anticipated by Nakayama *et al.* (WO 02/086071) because Nakayama *et al.* discloses a nucleotide sequence (SEQ ID NO: 7) that is 82.6% identical to the nucleotide sequence set forth as SEQ ID NO: 37. Applicants respectfully traverse this rejection. However, as discussed above, claim 15 is amended to recite that the isolated nucleic acid molecule “hybridizes under conditions of low stringency to a polynucleotide consisting of nucleotides 1-42 of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39.” As the Nakayama *et al.* sequence (SEQ ID NO: 7) aligns with SEQ ID NO: 37 beginning at residue 378 of SEQ ID NO: 37, the Nakayama *et al.* sequence does not hybridize to a polynucleotide consisting of residues 1-42 of SEQ ID NO: 37 (see sequence alignment presented with Office action), as required by amended claim 15. Thus, Nakayama *et al.* does not anticipate claim 15, as amended. Claims 16-17, 19-21, and 26-27 depend, directly or indirectly, from claim 15 and incorporate all of the limitations thereof. Applicants respectfully request that the rejection of claims 15-17, 19-21, and 26-27 be withdrawn in light of the current arguments and amendments.

Griffin *et al.* as evidenced by Blackshear *et al.*

Claims 5, 15-18, and 26-27 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Griffin *et al.*, as evidenced by Blackshear *et al.*, because Griffin *et al.* discloses an isolated human chromosome 12 and Blackshear *et al.* teaches that the gene is located on chromosome 12. Applicants strenuously traverse this rejection.

Claims 5, 15-18, and 26-27 relate to an **isolated** nucleic acid molecule. The specification clearly defines the term “isolated”, when used in relation to a nucleic acid, as “a nucleic acid sequence that is identified and separated from at least one contaminant nucleic acid with which it is ordinarily associated in its natural source. Isolated nucleic acid is present in a form or setting that is different from that in which it is found in nature. In contrast, **non-isolated** nucleic acids are nucleic acids such as DNA and RNA found in the state they exist in nature. For example, a given DNA sequence (*e.g.*, a gene) is found on the host cell chromosome in proximity to neighboring genes . . . However, **isolated** nucleic acid encoding RFX4_v3 includes, by way of example, such nucleic acid in cells ordinarily expressing RFX4_v3 where the nucleic acid is in a chromosomal location different from that of natural cells, or is otherwise flanked by a different nucleic acid sequence than that found in nature” (specification at page 20, lines 13-24; emphasis added).

Griffin *et al.* discloses a karyotype from a human patient which includes chromosome 12. Human chromosome 12 may include a nucleic acid sequence encoding a RFX4_v3 polypeptide or a nucleic acid molecule that hybridizes under conditions of low stringency to a polynucleotide consisting of nucleotides 1-42 of a nucleic acid sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39. However, as discussed above, the nucleic acid sequences disclosed in Griffin *et al.* are **non-isolated** as they are found on the host cell chromosome in proximity to neighboring genes. Thus, Applicants respectfully submit that Griffin *et al.* does not disclose an **isolated** nucleic acid molecule, as required by the claims and as defined in the specification. Applicants respectfully request the withdrawal of the rejection of claims 5, 15-18, and 26-27 on this ground.

Conclusion

Based on the foregoing amendments and arguments, the claims are in condition for allowance and notification to this effect is requested. If for any reason the Examiner believes that a telephone conference would expedite allowance of the claims, please telephone the undersigned at the number listed below.

Respectfully submitted,

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